REMARKS

Claims 1-49 were pending in this application. Claims 1-8 have been amended. Claims 13-49 have been canceled. New claims 50-59 have been added. Accordingly, upon entry of this amendment, claims 1-12 and 50-59 will be pending.

Any amendments to and/or cancellation of the claims are not to be construed as an acquiescence to any of the rejections set forth in the instant Office Action, and were done solely to expedite prosecution of the application. Applicants hereby reserve the right to pursue the subject matter of the claims as originally filed in this or a separate application(s).

Support for the amendments to the claims may be found throughout the specification and claims, as originally filed. *No new matter has been added.* Specifically, support for the amendments to claims 4 and 5 can be found, for example, at page 8, lines 1-4. Support for new claim 50 can be found, for example, at page 39, lines 4-8. Support for new claims 51 and 52 can be found, for example, at page 8, lines 28-35. Support for new claim 53 can be found, for example, at page 28, lines 19-22. Support for new claim 54 can be found, for example, at page 24, lines 8-10. Support for new claims 55 and 56 can be found at, for example, page 15, lines, 8-12. Support for new claim 57 can be found at, for example, page 37, lines 32-36. Support for new claim 58 can be found at, for example, page 18, lines, 8-23. Support for new claim 59 can be found at, for example, page 37, lines, 26-29.

Claim 15, 17, and 19 were omitted from the Restriction Requirement. Applicants assume the Examiner intended to include these claims in Groups III and XLII. Clarification by the Examiner is respectfully requested.

Election/Restriction

The Examiner has required restriction to one of the following inventions under 35 U.S.C. §121:

Groups I-XL are directed to human proteins or nucleic acids, and Groups XLI -LXXX are directed to mouse proteins or nucleic acids, respectively.

Group I. Claims 1, 2, 4, 6, and 8-12, drawn to an isolated nucleic acid encoding human T-bet protein, as well as vectors, host cells, and methods of producing the protein, classified in Class 536, subclass 23.5; Class 435, subclasses 69.1, 455, 252.3, and 320.1.

Group II. Claims 1, 3, 5, 7, and 8-12, drawn to an isolated nucleic acid encoding mouse T-bet protein, as well as vectors, host cells, and methods of producing the protein, classified in Class 536, subclass 23.5; Class 435, subclasses 69.1, 455, 252.3, and 320.1.

The following Groups of claims are directed to either human (Groups III - XLI) or mouse (Groups XLII - LXXX) proteins or nucleic acids.

Groups III and XLII. Claims 13, 14, 16, 18, and 20, drawn to and isolated T-bet protein, classified in Class 530, subclass 350.

Groups IV and XLIII. Claim 21, drawn to a fusion protein of T-bet, classified in Class 530, subclass 387.3.

Groups V and XLIV. Claims 22 - 25, drawn to antibodies to T-bet protein, classified in Class 530, subclass 387.1.

Groups VI and XLV. Claim 26, drawn to a nonhuman transgenic animal carrying a transgene encoding a T-bet protein, classified in Class 800, subclass 14.

Groups VII and XLVI. Claim 27, drawn to method for detecting the presence of T-bet in a biological sample, wherein the indicator comprises a T-bet protein and a DNA molecule to which it binds, classified in Class 435, subclass 6.

Groups VIII and XLVII. Claim 27, drawn to method for detecting the presence of T-bet in a biological sample, wherein the indicator is a cell comprising a T-bet protein and reporter gene, classified in Class 435, subclass 70.1.

Groups IX and XLVIII. Claims 28, 33, 35 - 37, and 39 - 42, drawn to a method for enhancing T-bet activity, wherein the step of contacting occurs in vivo, and wherein the agent is a T-bet nucleic acid molecule, classified in Class 514, subclass 44.

Groups X and XLVIX. Claims 28, 33, 35 - 37, and 39 - 42, drawn to a method for enhancing T-bet activity, wherein the step of contacting occurs in vivo, and wherein the agent is a T-bet peptide. classified in Class 514, subclass 21.

Groups XI and L. Claims 28, 33, 35 - 37, and 39 - 42, drawn to a method for enhancing T-bet activity, wherein the step of contacting occurs in vivo, and wherein the agent is a small molecule T-bet agonist, classified in Class 514, subclass 21.

Groups XII and LI. Claims 28, 33, 35 - 37, and 39 - 42, drawn to a method for enhancing T-bet activity, wherein the step of contacting occurs in vivo, and wherein the agent is a small molecule T-bet antagonist, classified in Class 514, subclass 21.

Groups XIII and LII. Claims 28, 33, 35 - 37, and 39 - 42, drawn to a method for enhancing T-bet activity, wherein the step of contacting occurs in vivo, and wherein the agent is an intracellular antibody, classified in Class 424, subclass 133.1.

Groups XIV and LIII. Claims 28, 33, 35 - 37, and 39 - 42, drawn to a method for enhancing T-bet activity, wherein the step of contacting occurs in vivo, and wherein the agent is an antisense nucleic acid molecule, classified in Class 514, subclass 44.

Groups XV and LIV. Claims 28, 33, 35 - 37, and 39 - 42, drawn to a method for enhancing T-bet activity, wherein the step of contacting occurs in vivo, and wherein the agent is a dominant negative T-bet molecule, classified in Class 514, subclass 21.

Groups XVI and LV. Claims 28, 33, 35 - 36, and 38 - 42, drawn to a method for enhancing T-bet activity, wherein the step of contacting occurs in vitro, and wherein the agent is a T-bet nucleic acid molecule, classified in Class 435, subclass 6.

Groups XVII and LVI. Claims 28, 33, 35 - 36, and 38 - 42, drawn to a method for enhancing T-bet activity, wherein the step of contacting occurs in vitro, and wherein the agent is a T-bet peptide, classified in Class 514, subclass 21.

Groups XVIII and LVII. Claims 28, 33, 35 - 36, and 38 - 42, drawn to a method for enhancing T-bet activity, wherein the step of contacting occurs in vitro, and wherein the agent is a small molecule T-bet agonist, classified in Class 514, subclass 21.

Groups XIX and LVIII. Claims 28, 33, 35 - 36, and 38 - 42, drawn to a method for enhancing T-bet activity, wherein the step of contacting occurs in vitro, and wherein the agent is a small molecule T-bet antagonist, classified in Class 435, subclass 6.

Groups XX and LVIX. Claims 28, 33, 35 - 36, and 38 - 42, drawn to a method for enhancing T-bet activity, wherein the step of contacting occurs in vitro, and wherein the agent is an intracellular antibody, classified in Class 424, subclass 133.1.

Groups XXI and LX. Claims 28, 33, 35 - 36, and 38 - 42, drawn to a method for enhancing T-bet activity, wherein the step of contacting occurs in vitro, and wherein the agent is an antisense nucleic acid molecule, classified in Class 435, subclass 6.

Groups XXII and LXI. Claims 28, 33, 35 - 36, and 38 - 42, drawn to a method for enhancing T-bet activity, wherein the step of contacting occurs in vitro, and wherein the agent is a dominant negative T-bet molecule, classified in Class 514, subclass 21.

Groups XXIII and LXII. Claims 28, 34, 35 - 37, and 39 - 42, drawn to a method for inhibiting T-bet activity, wherein the step of contacting occurs in vivo, and wherein the agent is a T-bet nucleic acid molecule, classified in Class 514, subclass 44.

Groups XXIV and LXIII, Claims 28, 34, 35 - 37, and 39 - 42, drawn to a method for inhibiting T-bet activity, wherein the step of contacting occurs in vivo, and wherein the agent is a T-bet peptide. classified in Class 514, subclass 21.

Groups XXV and LXIV. Claims 28, 34, 35 - 37, and 39 - 42, drawn to a method for inhibiting T-bet activity, wherein the step of contacting occurs in vivo, and wherein the agent is a small molecule T-bet agonist, classified in Class 514, subclass 21.

Groups XXVI and LXV. Claims 28, 34, 35 - 37, and 39 - 42, drawn to a method for inhibiting T-bet activity, wherein the step of contacting occurs in vivo, and wherein the agent is a small molecule T-bet antagonist, classified in Class 514, subclass 21.

Groups XXVII and LXVI. Claims 28, 34, 35 - 37, and 39 - 42, drawn to a method for inhibiting T-bet activity, wherein the step of contacting occurs in vivo, and wherein the agent is an intracellular antibody, classified in Class 424, subclass 133.1.

Groups XXVIII and LXVII. Claims 28, 34, 35 - 37, and 39 - 42, drawn to a method for inhibiting T-bet activity, wherein the step of contacting occurs in vivo, and wherein the agent is an antisense nucleic acid molecule, classified in Class 514, subclass 44.

Groups XXIX and LXVIII. Claims 28, 34, 35 - 37, and 39 - 42, drawn to a method for inhibiting T-bet activity, wherein the step of contacting occurs in vivo, and wherein the agent is a dominant negative T-bet molecule, classified in Class 514, subclass 21.

Groups XXX and LXIX. Claims 28, 34, 35, 36, and 38 - 42, drawn to a method for inhibiting T-bet activity, wherein the step of contacting occurs in vitro, and wherein the agent is a T-bet nucleic acid molecule, classified in Class 435, subclass 6.

Groups XXXI and LXX. Claims 28, 34, 35, 36, and 38 - 42, drawn to a method for inhibiting T-bet activity, wherein the step of contacting occurs in vitro, and wherein the agent is a T-bet peptide. classified in Class 514, subclass 21.

Groups XXXII and LXXI. Claims 28, 34, 35, 36, and 38 - 42, drawn to a method for inhibiting T-bet activity, wherein the step of contacting occurs in vitro, and wherein the agent is a small molecule T-bet agonist, classified in Class 514, subclass 21.

Groups XXXIII and LXXII. Claims 28, 34, 35, 36, and 38 - 42, drawn to a method for inhibiting T-bet activity, wherein the step of contacting occurs in vitro, and wherein the agent is a small molecule T-bet antagonist, classified in Class 514, subclass 21.

Groups XXXIV and LXXIII. Claims 28, 34, 35, 36, and 38 - 42, drawn to a method for inhibiting T-bet activity, wherein the step of contacting occurs in vitro, and wherein the agent is an intracellular antibody, classified in Class 424, subclass 133.1.

Groups XXXV and LXXIV. Claims 28, 34, 35, 36, and 38 - 42, drawn to a method for inhibiting T-bet activity, wherein the step of contacting occurs in vitro, and wherein the agent is an antisense nucleic acid molecule, classified in Class 435, subclass 6.

Groups XXXVI and LXXV. Claims 28, 34, 35, 36, and 38 - 42, drawn to a method for inhibiting T-bet activity, wherein the step of contacting occurs in vitro, and wherein the agent is a dominant negative T-bet molecule, classified in Class 514, subclass 21.

Groups XXXVII and LXXVI. Claims 29, 30, 32, 33, and 35 - 42, drawn to a method for identifying compounds that enhance the activity of T-bet protein, wherein the indicator composition comprises a T-bet protein and a DNA molecule to which it binds, classified in Class 435, subclass 6.

Groups XXXVIII and LXXVII. Claims 29, 31 - 33, and 35 - 42, drawn to a method for identifying compounds that enhance the activity of T-bet protein, wherein the indicator

composition is a cell comprising a T-bet protein and reporter gene, classified in Class 435, subclass 70.1.

Groups XXXIX and LXXVIII. Claims 29, 30, 32 and 34 - 42, drawn to a method for identifying compounds that inhibit the activity of T-bet protein, wherein the indicator composition comprises a T-bet protein and a DNA molecule to which it binds, classified in Class 435, subclass 6.

Groups XL and LXXIX. Claims 29, 31, 32 and 34 - 42, drawn to a method for identifying compounds that inhibit the activity of T-bet protein, wherein the indicator composition is a cell comprising a T-bet protein and reporter gene, classified in Class 435, subclass 70.1.

Groups XLI and LXXX. Claims 43 - 49, drawn to a method of diagnosing a subject based on a change in expression of T-bet protein, classified in Class 435, subclass 7.1.

In addition, the Examiner states that the application contains claims directed to the following patentably distinct species and requires election of one species from the following categories:

Inventions XIII - XXXXIV, wherein the activity of T-bet is:

(A) IFN-y production, or

(B) transcription of lgG2a.

Inventions XIII - XXXXIV, wherein the cell is:

(A) a T cell,

(B) a B cell, or

(C) a macrophage.

Invention XXXXV, wherein the disorder is:

(A) lupus

(B) Inflammatory Bowel Disease,

(C) Crohn's disease,

(D) ulcerative colitis, or

(E) asthma.

The Examiner states that "The claims are drawn to nucleic acids, proteins, antibodies and methods relating to either human or mouse T-bet proteins. These proteins vary in composition and possess different structures, sequences, and properties, which require non-coextensive searches in the scientific literature." "Consequently, the restriction has been set forth for claims directed to human and mouse molecules as different groups, irrespective of the format of the claims."

The Examiner continues and states that "[c]laims 27, 29-31, and dependent claims thereof are drawn to the following patentably distinct inventions, wherein the indicator or indicator composition comprises either a combination of T-bet protein with a DNA molecule to which the T-bet protein binds, or a cell comprising a T-bet protein and a reporter gene. These products are distinct because their structures, physiochemical properties and mode of action are different."

With respect to claims 28 and 29, the Examiner states that these claims "contain recitations of methods which include the step of 'contacting', while dependent claims 37 and 38 contain recitation of 'contacting' occurring either *in vivo* or *in vitro*. These methods are distinct in that they differ in method steps. Therefore, the restriction has been set forth for claims directed to methods involving contacting *in vivo* or *in vitro* as different groups, irrespective of the format of the claims."

The Examiner also states that "[c]laim 28 contains a recitation of an 'agent', while dependent claims 39 and 40 contain recitation of agents which include a T-bet nucleic acid molecule, a T-bet peptide, a T-bet agonist or antagonist, an intracellular antibody, an antisense nucleic acid molecule, or a dominant negative T-bet molecule. These agents are distinct because their structures, physiochemical properties and mode of action are different."

Applicants' respectfully traverse the foregoing Restriction Requirement and submit that the requirement is improper. Applicants' grouns for traversal are set forth below.

At the outset, Applicants point out that Groups XII, LI, XIII, LII, XIV, LIII, XV, LIV, XIX, LVIII, XX, LVIX, XXI, LX, XXII, LXI should be removed from the restriction requirement as the claims are directed to methods of enhancing T-bet activity and the Examiner has required election among species which ***downmodulate*** T-bet activity. Similarly, Groups XXIII, LXII, XXIV, LXII, XXV, LXIV, XXX, LXIX, XXXI, LXX, XXXII, LXXI should be removed from the restriction requirement as the claims are directed to methods of inhibiting T-bet activity and the Examiner has required election among species that ***enhance*** T bet activity.

In addition, with respect to the Examiner's grouping of human and murine nucleic acids, proteins, and methods of their use into different groups, in contrast to the Examiner's statements, the human and murine T bet nucleic acid molecules and human and murine protein molecules are structurally related. The nucleic acid molecules share 85.7% identity and the amino acid molecules share 86.9% identity. In addition, these human and murine molecules share a common function, binding to T box binding domains present in DNA. Accordingly, Applicants submit that the human Groups (III-XLI) and murine Groups (XLII-LXXX) formed by the Examiner should be rejoined and a species election required for search purposes.

In order to be considered responsive to the instant Office Action, Applicants' hereby elect Group I (claims 1, 2, 4, 6, and 8-12) ***with traverse***. Applicants traverse the restriction requirement to the extent that Groups I and II should be reformed as a single group containing claims 1-12 (referred to hereinafter as "***newly formed Group I***").

Applicants have presented allowable generic linking claims, claims 51 and 52, which embrace the species of human and murine T-bet nucleic acid molecules as these molecules hybridize to each other under stringent conditions based on their level of nucleotide sequence identity. It is Applicants position that given the presence of claims 51 and 52, a restriction under 35 U.S.C. §121 is improper. Applicants respectfully submit that while a species election may be proper among human and mouse T bet nucleic acid molecules for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable, an election under 35 U.S.C. §121 as proposed by the Examiner is improper since the claims are linked by allowable generic linking claims, claims 51 and 52, which embrace the species of human and murine T-bet nucleic acid molecules.

Moreover, Applicants respectfully submit that the search of nucleic acid molecules encoding murine T-bet proteins (claims 1, 2, 4, 6, and 8-12) would be coextensive with a search for nucleic acid molecules encoding human T-bet proteins (claims 1, 3, 5, 7, and 8-12), and would not place a burden on the Examiner. As the M.P.E.P. states:

> [i]f the search and examination of an entire application can be made without serious burden, the examiner must examine it on the merits, even though it includes claims to independent or distinct inventions. M.P.E.P. § 803.

If a species election is required, Applicants elect the species of ***human*** T-bet nucleic acid molecules for search purposes.

Furthermore, with regard to the unelected groups, Applicants submit that Groups III and IV and Groups XLII and XLIII should be reformed as a single group containing claims 13-21. Claim 13 is an allowable generic claim which embraces the species of human and murine T-bet polypeptides (including fusion proteins) and is generic to the groups set forth by the Examiner based on their level of amino acid identity and common function, as discussed above.

Applicants also submit that Groups VII and XLVI and Groups VIII and XLVII should be reformed as a single group containing claim 27. Claim 27 is drawn to a method for detecting the presence of T-bet in a biological sample. Claim 27 is an allowable generic claim, which embraces the species of an indicator composition comprising a T-bet protein and a DNA molecule, and as well as the species of an indicator composition comprising a cell comprising a T-bet protein and a reporter gene, which is generic to the groups set forth by the Examiner.

With respect to Groups IX-XXV and XLVIII-LIV and Groups XXIII-XXIX and LXII-LXVII, Applicants submit that claim 28 is an allowable generic claim, which is generic to the groups set forth by the Examiner. Claim 28 is drawn to a method of modulating T-bet activity (*e.g.,* enhancing T-bet activity or inhibiting T-bet activity) in a cell, comprising contacting a cell with a compound that modulates T-bet activity.

Similarly, with respect to Groups XVI-XXII and LV-LXI and Groups XXX-XXXVI and LXIX-LXXV, Applicants submit that claim 28 is an allowable generic claim, which is generic to the groups set forth by the Examiner. Claim 28 is drawn to a method of modulating T-bet

activity (*e.g.*, enhancing T-bet activity or inhibiting T-bet activity), comprising contacting a cell with a compound that modulates T-bet activity.

Applicants also submit that claim 29 is an allowable generic claim that is generic to Groups XXXVII and LXXVI and Groups XXXVIII and LXXXVII, as well as to Groups XXXIX and LXXVIII and Groups XL and LXXIX as set forth by the Examiner. Claim 29 is drawn to a method of identifying an agent that modulates the activity of a T-bet protein (*e.g.*, enhancing the activity of a T-bet or inhibiting the activity of a T-bet protein). Claim 29 embraces the species of identifying an agent that enhances T-bet activity comprising a T-bet nucleic acid molecule, identifying an agent that enhances T-bet activity comprising a T-bet peptide, and identifying an agent that enhances T-bet activity comprising a T-bet agonist. Claim 29 also embraces the species of identifying an agent that inhibits T-bet activity comprising a T-bet antagonist, identifying an agent that inhibits T-bet activity comprising a T-bet intracellular antibody, identifying an agent that inhibits T-bet activity comprising a T-bet antisense nucleic acid molecule and identifying an agent that inhibits T-bet activity comprising a dominant-negative T-bet molecule.

CONCLUSION

If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call Applicants' Attorney at (617) 227-7400.

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Respectfully submitted,

By _____

Megan E. Williams
Registration No.: 43,270
LAHIVE & COCKFIELD, LLP
28 State Street
Boston, Massachusetts 02109
(617) 227-7400
(617) 742-4214 (Fax)
Attorney/Agent For Applicant